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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,875	02/25/2004	Gary J. Latham	AMBI:089US	1898

62619 7590 07/28/2006

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EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,875	LATHAM ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38,45-49,57-68,74 and 82-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *109,111 and 112* is/are allowed.

6)☒ Claim(s) *1-38, 45-49, 57-68, 74 ,82-108 and 110* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

1. The applicant's response (filed 16 MAY 06) to the Office Action has been entered. Following the entry of the claim amendment(s), **Claim(s) 1-38, 45-49, 57-68, 74 and 82-112** is/are pending. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

35 USC § 112- 2nd Paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

3. **Claim(s) 1-38, 45-49, 57-68, 74, 82-108** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7-9, 21, 23, 26, 45, 49, 57-59, 64-65 and 74 are indefinite in light of the phrase "small molecule." "Small" is a relative term. It is therefore impossible to determine the scope of the claimed invention. As regards, Claim 1 for example, how large must the organic molecule comprising a nitrogenous base, an inorganic compound, a salt or an aromatic structure be to be considered a non-small molecule (i.e. outside the scope of the claimed invention)?

One reading of **Claim 1** is "wherein the first nuclease inhibitor is a small organic molecule/compound comprising an inorganic compound." The scope of what is intended is unclear. For example, does β-mercaptoethanol meet this limitation? The

chemical structure of β-mercaptoethanol can be seen at : http://www.piercenet.com/Products/Browse.cfm?fldID=02040904.

β-mercaptoethanol is a small organic molecule/compound (i.e. a compound comprising Carbon and Hydrogen) which comprises an inorganic compound SH. For this reading a compound is defined as is a chemical substance consisting of two or more different chemically bonded chemical elements with a fixed ratio determining the composition.

35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

CLAIM REJECTIONS UNDER 35 USC § 102

6. Claim(s) 1-16, 19-21, 23-27, 30-33, 45, 83, 85-87, 89-92 and 110 is/are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al. [Section 5-2, 11-1 and 11-2 (1986)].

a. Davis et al. teach a RNA extraction method "Mini Method" Section 11-2, which utilizes a first nuclease inhibitor (i.e. phenol) which is a small organic molecule comprising an aromatic structure and second nuclease inhibitor (vanadyl ribonuclease complex, SDS, heparin or EDTA). Davis et al. in Section 11-2 teach a method/solution comprising all of the limitations recited in **Claim 1, 3-9, 11-16, 19-20, 83 and 92**. See steps 1-3.

The chemical structure of phenol can be seen at http://en.wikipedia.org/wiki/Phenol. Also phenol can be classified as a chaotrope (i.e. a chemical compound which denatures proteins. As regards Claims 7-16 and 85-86 note the Material Safety data sheet for vanadyl ribonuclease which can be found at the New England Biolabs website. Note especially the structure of VRC shown therein.

b. If you reverse the inhibitors [i.e. wherein the first nuclease is (vanadyl ribonuclease complex] and the second nuclease inhibitor is SDS, heparin, EDTA or phenol then Section 11-2 reads on the method(s)/solution recited in **Claims 1-10, 15-16, 19-20, 45, 83, 85-86 and 110.** Note that vanadyl ribonuclease complex is a small organic molecule comprising a nitrogenous base. VRC functions as a competitive inhibitor comprising a ribonucleoside

The structure of EDTA can be seen at http://en.wikipedia.org/wiki/EDTA. The structure of SDS can be seen at http://en.wikipedia.org/wiki/Sodium_dodecyl_sulfate. The structure of heparin can be seen at http://en.wikipedia.org/wiki/Heparin. Also note that phenol is a hydrophobic organic compound.

c. If β-mercaptoethanol meets the limitation(s) of the first nuclease inhibitor,

note the 112, 2nd paragraph rejection recited above, then that portion of the RNA extraction method set forth in Section 11-1 of Davis et al. wherein GIT buffer is utilized reads on a method/solution comprising all of the limitations recited in **Claims 1-9, 11, 26-27 and 83**. Here the first nuclease inhibitor is 2-ME (i.e. β-mercaptoethanol) and the second nuclease inhibitor is guanidine isothiocyanate which is a synonym for guanidinium thiocyanate] Note also that these two nuclease inhibitors are mixed together (i.e. forming the GIT buffer) before mixing with the composition (i.e. the cellular pellet).

d. If you consider the first nuclease inhibitor to be proteinase K and the second nuclease inhibitor to be EDTA, NaCl, SDS or phenol, then Davis et al. in Section 11-1 at steps 19-24 (see especially the PK buffer) teach a method(s)/solution comprising all of the limitations of **Claims 1, 3-12, 15-16, 19-21, 23-26, 83.** In addition Davis et al. in Section 11-1 at steps 19-24 teach all of the limitations of method recited in **Claim 87, 89-91**. Here the first nuclease inhibitor is NaCl and the second nuclease inhibitor is EDTA, SDS, proteinase K or phenol.

e. Davis et al. also teach in Section 5-2 a method/solution comprising all of the limitations recited in **Claim 1-4, 6-10, 12, 15-16 and 19-21, 23-26, 45, 83 and 92.** Here the first nuclease inhibitor (i.e. proteinase K) is a small organic molecule comprising an aromatic structure. See the amino acid sequence of Proteinase K in Samal et al. [US 5,278,062 (1994)] Figures 4A-4 –4C and note especially the presence of phenylalanine (F) and tyrosine (Y) residues. These amino acids comprise an aromatic side chain, therefore it can be said that Proteinase K is a small organic compound comprising an aromatic structure. Note also that three second nuclease inhibitors (i.e. EDTA, NaCl, SDS) are mixed with proteinase K before mixing with the composition (i.e. the cellular pellet). If you consider the inorganic monovalent salt NaCl to be the first nuclease inhibitor then Section 5-2 of Davis et al., also teaches a method comprising all of the limitations recited in **Claim 87 and 89-91.**

f. Note also the steps involved in cleaning the DNA (i.e. steps 6-13 of section 5-2). There another second nuclease inhibitor (i.e. phenol) is mixed with the composition comprising Proteinase K, EDTA, NaCl and SDS. This section reads on

Claims 87, 89-91 if you consider the first nuclease inhibitor to be NaCl and the second nuclease inhibitor to be any of Proteinase K, EDTA, SDS or phenol.

g. In Section 5-2, if phenol is considered to be the first nuclease inhibitor and Proteinase K, EDTA, NaCl or SDS are taken to be the second nuclease inhibitor then Section 5-2 of Davis et al. teaches a method comprising all of the limitations recited in **Claim 1, 3-4, 6-9, 12, 15-16, 19-21, 23-25, 30-33, 45 and 92**.

h. Finally, see Section 5-3 of Davis et al. Here Davis et al. teach a method/solution all of the limitations of **Claim 1, 3-4, 6-9, 12, 15-16, 19-21, 23-25, 30-33, 45, 83 and 92** when phenol is considered to be the first nuclease inhibitor and one of EDTA, NaCl, SDS or Proteinase K is considered to be the second nuclease inhibitor.

i. Alternatively, if Proteinase K is considered to be the first nuclease inhibitor and one of EDTA, NaCl, SDS or phenol is considered to be the second nuclease inhibitor then Section 5-3 of Davis et al. reads on **Claims 1, 3-4, 6-10, 15-16, 19-21, 23-26 and 45.** This section also reads on **Claims 87, 89-91** if you consider the first nuclease inhibitor to be NaCl and the second nuclease inhibitor to be any of Proteinase K, EDTA, SDS or phenol.

7. Claim(s) 1, 3-12, 15-18, 21-25, 82-83 and 87-91 is/are rejected under 35 U.S.C. 102(b) as being anticipated by Kondo et al. [US 5,470,971 (1995)].

Kondo et al. teach a method which comprises obtaining a composition which composition comprises first (placental ribonuclease inhibitor) and second nuclease inhibitor(s) (DTT, $MgCl_2$, EDTA, ethanol). See at least for example the paragraph bridging Column 28-29. Please note that placental ribonuclease inhibitor (i.e. RNasin) is a small organic compound / proteinaceous compound comprising an aromatic structure. See the primary structure of human placental ribonuclease inhibitor on p.8547 of Lee et al. [Biochemistry 27 : 8545-8553 (1988)]. Note especially the presence of phenylalanine (F) and tyrosine (Y) residues. These amino acids comprise an aromatic side chain, therefore it can be said that human placental ribonuclease

inhibitor is a small organic compound comprising an aromatic structure. The structure of DTT can be seen at http://en.wikipedia.org/wiki/Dithiothreitol

Note that Kondo et al. also teach adding KCl an inorganic compound/a monovalent salt and $MgCl_2$ an inorganic compound/metallic complex/ multivalent salt to their admixture. As such, Kondo et al. read on a method/solution comprising all of the limitations of **Claim 1, 3-12, 15-18, 21-25 and 82-83.** Kondo et al. also teach a method comprising all of the limitations recited in **Claim 87-91** when $MgCl_2$ or KCl are the "first" nuclease inhibitors.

8. **Claim(s) 1-10, 12, 15-18, 82-83 and 92** is/are rejected under 35 U.S.C. 102(b) as being anticipated by Robbi et al. [PNAS 75(9) : 4344-4348 (1978)].

Robbi et al. teach *in vitro* translation wherein human placental ribonuclease inhibitor (i.e. RNasin) is utilized . As argued above, human placental ribonuclease inhibitor is a small organic molecule comprising an aromatic structure. Note also that Robbi et al. teach that the Rnasin used (i.e. prior to its addition to the cell free protein synthesizing composition) was in a buffer comprising DTT and EDTA (both of which are nuclease inhibitors). Robbi et al. teach a method comprising all of the limitations of **Claim 1-10, 12, and 15-18, 82-83 and 92**.

35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

11. **Claim(s) 84** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. [Section 5-2, 11-1 and 11-2 (1986)] or Kondo et al. [US 5,470,971 (1995)].or Robbi et al. [PNAS 75(9) : 4344-4348 (1978)] or as applied against Claim 1 above and further in view of The Stratagene Catalog p.39 (1988).

Each of the primary references teach a method and the reagents necessary to perform their method(s) comprising all of the limitations of Claim 1 and 84. The primary references do not teach assembling all of the reagents for performing their method(s) into a kit. However, as evidenced by the Stratagene Catalog teaching, it was well known at the time of the invention to place the reagents needed to perform a nucleic acid based methods into a kit format. In addition, the Stratagene catalog teaches the advantages of assembling a kit, such as, saving resources and reducing waste. Therefore, absent an unexpected result, it would have been *prima facie* obvious to the ordinary artisan at the time of the invention to modify the teachings of any of the primary references with the teachings of the Stratagene Catalog wherein the reagents necessary to perform the method(s) taught by the primary references are placed into a kit format. The ordinary artisan would have been motivated to make this modification in order to take advantage of the savings and efficiency afforded by kits.

REASON FOR ALLOWANCE

12. **Claim(s) 109, and 111-112** are allowable over the prior art of record because the prior art considered does not teach or reasonably suggest, either alone or in combination with the other prior art considered the method(s) recited in Claim 109 and 111.

CLAIM OBJECTIONS

13. **Claim(s) 28-29, 34-38, 46-49, 57-68, 74, and 93-108** is/are objected to because it/ they are dependent upon a rejected independent base claim.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

14. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

15. **Claim(s) 109 and 111-112** is/are allowable while Claim(s) **1-38, 45-49, 57-68, 74, 82-108 and 110** is/are rejected and/or objected to for the reason(s) set forth above.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM - 5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

ETHAN WHISENANT
PRIMARY EXAMINER
Art Unit 1634